UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,769	06/27/2006	Sam Philip Heywood	07-1048-WO-US	7843

20306 7590 02/18/2010

MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
02/18/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,769	HEYWOOD ET AL.	
	Examiner	Art Unit	
	DAVID J. BLANCHARD	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-7,21-38,43,45,46 and 48-56* is/are pending in the application.

4a) Of the above claim(s) *21-23 and 30-38* is/are withdrawn from consideration.

5)☒ Claim(s) *5-7* is/are allowed.

6)☒ Claim(s) *24-29,43,45,46 and 48-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/13/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-4, 8-20, 39-42, 44 and 47 are cancelled.

Claims 24-25 and 45-46 have been amended.

Claims 48-56 have been added.

3. Claims 21-23 and 30-38 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

4. Claims 5-7, 24-29, 43, 45-46 and 48-56 are under consideration.

5. This Office Action contains New Grounds of Rejections.

Information Disclosure Statement

6. The Information Disclosure Statement (IDS) filed 13 November 2009 has been considered by the Examiner. A signed and initialed copy of the IDS is included with the instant Office Action.

Objections/Rejections Withdrawn

7. The rejection of claims 24-29, 41, 43 and 47 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation "derivative thereof" in claims 24 and 41 is withdrawn in view of the amendments to the claims.

8. The rejection of claims 45-46 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation "2 X 20,000 Da PEG", "3 X 20,000 Da PEG" and "2 X 30,000 Da PEG" is withdrawn in view of the amendments to the claims.

9. The rejection of claims 41 and 47 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as introducing new matter is withdrawn in view of the cancellation of the claims.

10. The rejection of claims 24-29, 41 43 and 45-47 under 35 U.S.C. 103(a) as being unpatentable over Singh et al (Analytical Biochemistry, 304(2):147-156, May 15, 2002, cited on

PTO-892 mailed 2/26/2008) in view of Hesi et al (WO 98/37200, 8/27/1998, IDS reference 41 filed 10/20/06) and Humphreys D. P. (WO 99/15549, 4/1/1999, IDS reference 42 filed 10/20/06) is withdrawn in view of the amendments to the claims and the cancellation of the claims 41 and 47.

11. The rejection of claims 24-29, 41, 43 and 45-47 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7 and 10 of U.S. Patent No. 6,642,356 B1 in view of Singh et al (Analytical Biochemistry, 304(2):147-156, May 15, 2002, cited on PTO-892 mailed 2/26/2008) in view of Hesi et al (WO 98/37200, 8/27/1998, IDS reference 41 filed 10/20/06) and Humphreys D. P. (WO 99/15549, 4/1/1999, IDS reference 42 filed 10/20/06) is withdrawn in view of the amendments to the claims and the cancellation of the claims 41 and 47.

Rejections Maintained and New Grounds of Objections/Rejections

Claim Objections

12. Claim 26 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form. Base claim 24 recites that one PEG molecules is attached to the interchain cysteine of the CL and the interchain cysteine of the CH1 has been replaced by another amino acid, whereas claim 26 recites that one effector molecule is attached to the interchain cysteine of the light chain and the interchain cysteine of the heavy chain, which would otherwise be linked to each other via a disulfide bond if the effector molecules were not attached. Thus, dependent claim 26 which requires the presence of both interchain cysteines does not incorporate all the limitations of the base claim, e.g., where the interchain cysteine of the CH1 is replaced by another amino acid according to base claim 24. Applicant is reminded that any claim which is in dependent form but which is so worded that it, in fact is not, as, for example, it does not include every limitation of the claim on which it depends, will be required to be canceled as not being a

proper dependent claim; and cancellation of any further claim depending on such a dependent claim will be similarly required.

13. Claims 45-46 and 53-54 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form. Base claims 24 and 48 from which claims 45-46 (base claim 24) and 53-54 (base claim 48) depend recite that the PEG molecules have a molecular weight in the range of 5,000 to 30,000 Da, whereas claims 45-46 and 53-54 recite that each of the PEG molecules are 20,000 Da or larger. Thus, claims 45-46 and 53-54 exclude the lower end of the range of the base claims and include molecular weights above the range required by the base claims and as such do not include every limitation of the base claims. Applicant is reminded that any claim which is in dependent form but which is so worded that it, in fact is not, as, for example, it does not include every limitation of the claim on which it depends, will be required to be canceled as not being a proper dependent claim; and cancellation of any further claim depending on such a dependent claim will be similarly required.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. The rejection of claims 24-29, 43, 45-46 and now applied to newly added claims 48-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained and made again. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The response filed 2/26/2009 and now 11/13/2009 introduces NEW MATTER into the claims. As presently amended claim 24 and newly added claims 48, 55 and 56 recite that the at

least two PEG effector molecules of the antibody Fab or Fab' fragment have an average molecular weight in the range from 5,000 to 30,000 Da. Further, as presently amended, claims 45-46 and newly added claims 53-54 recite wherein each PEG has a molecular weight of 20,000 Da or larger, or 30,000 Da or larger. The responses filed 2/26/2009 and now 11/13/2009 do not point out where support for presently amended claim 24 and newly added claims 48, 55 and 56 could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 ("Applicant should therefore specifically point out the support for any amendments made to the disclosure."). Page 8 of the as filed specification discloses various ranges of the polymer, including the broader range 5,000 to 40,000 Da, however, this does not provide adequate written support for the newly presented narrower range of 5,000 to 30,000 Da. Similarly, there is no disclosure of the broader range of 20,000 Da or larger and 30,000 Da or larger, each of which do not have an upper limit. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972). Further, the claims as presently amended and newly added recite "at least two effector molecules, wherein each effector molecule is a PEG..", which is broader than the previous recitation of two or three effector molecules. The recitation "at least two effector molecules…" does not contain an upper limit and as such embraces five, eight, ten, or more PEG molecules attached to the Fab or Fab' fragments, which is not clearly supported in the as filed disclosure.

As presently amended and newly added claims 24-29, 43, 45-46 and now newly added claims 48-56 now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the presently amended and newly added claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in the present claims in the specification or claims, as filed, or remove these limitations from the claims in response to this Office Action.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 24-25, 27-29, 43, 45-46 and 48-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapman et al (Nature Biotechnology, 17:780-783, 1999, IDS reference 4 filed 10/20/06) in view of Hesi et al (WO 98/37200, 8/27/1998, IDS reference 41 filed 10/20/06) and Humphreys D. P. (WO 99/15549, 4/1/1999, IDS reference 42 filed 10/20/06).

Chapman et al teach that the random attachment of PEG to Fab' fragments results in conjugate heterogeneity and reduced antigen binding, however, Chapman et al teach that site-specific attachment of PEG molecules (e.g., PEG-maleimide of 5 kDa, 25 kDa and 40 kDa) to Fab' fragments at one or two engineered hinge cysteine residues retain full antigen-binding activity, have increased *in vivo* half-lives, improved pharmacokinetic profiles over whole IgG

and the use of one or two defined PEG attachment sites facilitates the production of well-defined conjugates that are identical from batch to batch and simple to scale up and should allow for rapid and economic production of therapeutic antibodies for chronic disease therapy (see entire document, particularly abstract, and pp. 780-781). Chapman et al do not specifically teach wherein one the interchain cysteine of the CH1 (residue 233) or CL (residue 214) of the Fab' fragments is mutated to serine and the remaining interchain cysteine is attached to PEG or wherein the modified hinge region comprises the recited sequences. These deficiencies are made up for in the teachings of Hesi et al and Humphreys et al.

Hesi et al teach anti-IL-8 Fab, Fab' and Fab-SH fragments for the treatment of inflammatory disorders wherein the antibody fragments may be conjugated to a polyethylene glycol (PEG) molecule via a cysteine residue in the light or heavy chain of the antibody fragment that would ordinarily form the disulfide bridge linking the light and heavy chains wherein the disulfide bridge is avoided by substituting one of the interchain cysteines for another amino acid, such as serine, wherein each PEG molecule may be 20,000 Da or 30,000 Da as well as pharmaceutical compositions comprising the anti-IL-8 antibody fragments and a pharmaceutically acceptable carrier, excipient or stabilizer (see entire document, particularly pp. 21-38 and 104-105).

Humphreys teach the known Fab' hinge region peptides that are well tolerated in *E.coli* and are non-immunogenic and the hinge region peptides of Humphreys are identical to the hinge regions of SEQ ID Nos:1-3 (see entire document, particularly pp. 2 and Table II).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced anti-IL-8 Fab or Fab' fragments comprising a hinge region having one or two cysteines (e.g., SEQ ID Nos:1-3) and wherein one or the interchain cysteines (CH1 or CL) is mutated to a serine and wherein the hinge cysteine(s) and the interchain cysteine (CH1 or CL) are PEGylated, as well as pharmaceutical compositions comprising the PEGylated anti-IL-8 Fab or Fab' fragments and a pharmaceutically acceptable carrier or excipient for therapeutic benefit of inflammatory disorders.

One of ordinary skill in the art would have been motivated and had a reasonable expectation of success at the time the invention was made to have produced anti-IL-8 Fab or Fab' fragments comprising a hinge region having one or two cysteines (e.g., SEQ ID Nos:1-3) and

wherein one or the interchain cysteines (CH1 or CL) is mutated to a serine and wherein the hinge cysteine(s) and the interchain cysteine (CH1 or CL) are PEGylated, as well as pharmaceutical compositions comprising the PEGylated anti-IL-8 Fab or Fab' fragments and a pharmaceutically acceptable carrier or excipient for therapeutic benefit of inflammatory disorders in view of Chapman et al and Hesi et al and Humphreys because Chapman et al teach that the random attachment of PEG to Fab' fragments results in conjugate heterogeneity and reduced antigen binding, however, Chapman et al teach that site-specific attachment of PEG molecules (e.g., PEG-maleimide of 5 kDa, 25 kDa and 40 kDa) to Fab' fragments at one or two engineered hinge cysteine residues retain full antigen-binding activity, have increased *in vivo* half-lives, improved pharmacokinetic profiles over whole IgG and the use of one or two defined PEG attachment sites facilitates the production of well-defined conjugates that are identical from batch to batch and simple to scale up and should allow for rapid and economic production of therapeutic antibodies for chronic disease therapy and Hesi et al teach anti-IL-8 Fab, Fab' and Fab-SH fragments for the treatment of inflammatory disorders wherein the antibody fragments may be conjugated to a polyethylene glycol (PEG) molecule via a cysteine residue in the light or heavy chain of the antibody fragment that would ordinarily form the disulfide bridge linking the light and heavy chains wherein the disulfide bridge is avoided by substituting one of the interchain cysteines for another amino acid, such as serine, wherein each PEG molecule may be 20,000 Da or 30,000 Da as well as pharmaceutical compositions comprising the anti-IL-8 antibody fragments and a pharmaceutically acceptable carrier, excipient or stabilizer and Humphreys teach known Fab' hinge region peptides (identical to instantly claimed SEQ ID Nos:1-3), which are well tolerated in *E.coli* and are non-immunogenic. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to produce site-specific PEGylated aniti-IL-8 Fab or Fab' fragments containing the hinge peptides of Humphreys (e.g., identical to SEQ ID Nos:1, 2 or 3) and wherein one of the interchain cysteines (CH1 or CL) is mutated to a serine leaving the remaining interchain cysteine and the hinge cysteine(s) available for site-specific PEG attachment since site-specific attachment of PEG molecules retains full antigen-binding activity, increased *in vivo* half-lives, improved pharmacokinetic profiles over whole IgG and the use of defined PEG attachment sites facilitates the production of well-defined conjugates that are identical from batch to batch and simple to scale up, allowing for rapid and economic production

of therapeutic antibodies for chronic disease, thereby overcoming conjugate heterogeneity and reduced antigen binding associated with random attachment of PEG to Fab and Fab' fragments according to Chapman et al. Thus, there would be several advantages to producing anti-IL-8 Fab and Fab' fragments modified by site-specific attachment of PEG molecules at one of the interchain cysteines (CH1 or CL) and cysteine(s) within the hinge region (e.g., SEQ ID NO:1, 2 or 3), particularly for therapeutic benefit of inflammatory disorders. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced anti-IL-8 Fab or Fab' fragments comprising a hinge region having one or two cysteines (e.g., SEQ ID Nos:1-3) and wherein one or the interchain cysteines (CH1 or CL) is mutated to a serine and wherein the hinge cysteine(s) and the interchain cysteine (CH1 or CL) are PEGylated, as well as pharmaceutical compositions comprising the PEGylated anti-IL-8 Fab or Fab' fragments and a pharmaceutically acceptable carrier or excipient for therapeutic benefit of inflammatory disorders in view of Chapman et al and Hesi et al and Humphreys.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 24-25, 27-29, 43, 45-46 and 48-56 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7 and 10 of U.S. Patent No. 6,642,356 B1 in view of Chapman et al (Nature Biotechnology, 17:780-783, 1999, IDS reference 4 filed 10/20/06) and Hesi et al (WO 98/37200, 8/27/1998, IDS reference 41 filed 10/20/06) and Humphreys D. P. (WO 99/15549, 4/1/1999, IDS reference 42 filed 10/20/06).

Claims 7 and 10 of U.S. Patent No. 6,642,356 B1 are drawn to a Fab or Fab' fragment comprising one polypeptide chain that comprises the amino acid sequence of SEQ ID NO:1 (e.g., TCPPCPXYCPPCPA), wherein X and Y are neutral aliphatic L-amino acid residues and wherein the Fab or Fab' fragment has one or more effector or reporter molecules attached to it. Claims 7 and 10 of U.S. Patent No. 6,642,356 B1 do not specifically teach wherein one the interchain cysteine of the CH1 (residue 233) or CL (residue 214) is mutated to serine and the remaining interchain cysteine is attached to PEG or wherein the modified hinge region comprises the recited sequences wherein PEG is attached to at least one hinge cysteine. These deficiencies are made for in the teachings of Chapman et al and Hesi et al and Humphreys et al.

Chapman et al have been described supra.

Hesi et al have been described supra.

Humphreys et al have been described supra.

The claims in the instant application are obvious variants of claims 7 and 10 of U.S. Patent No. 6,642,356 B1 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced Fab or Fab' fragments comprising a hinge region having one or two cysteines (e.g., SEQ ID Nos:1-3) and wherein one

or the interchain cysteines (CH1 or CL) is mutated to a serine and wherein the hinge cysteine(s) and the interchain cysteine (CH1 or CL) are PEGylated, as well as pharmaceutical compositions comprising the PEGylated Fab or Fab' fragments and a pharmaceutically acceptable carrier or excipient.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced Fab or Fab' fragments comprising a hinge region having one or two cysteines (e.g., SEQ ID Nos:1-3) and wherein one or the interchain cysteines (CH1 or CL) is mutated to a serine and wherein the hinge cysteine(s) and the interchain cysteine (CH1 or CL) are PEGylated, as well as pharmaceutical compositions comprising the PEGylated Fab or Fab' fragments and a pharmaceutically acceptable carrier or excipient in view of claims 7 and 10 of U.S. Patent No. 6,642,356 B1 and Chapman et al and Hesi et al and Humphreys because Chapman teach that the random attachment of PEG to Fab' fragments results in conjugate heterogeneity and reduced antigen binding, however, Chapman et al teach that site-specific attachment of PEG molecules (e.g., PEG-maleimide of 5 kDa, 25 kDa and 40 kDa) to Fab' fragments at one or two engineered hinge cysteine residues retain full antigen-binding activity, have increased *in vivo* half-lives, improved pharmacokinetic profiles over whole IgG and the use of one or two defined PEG attachment sites facilitates the production of well-defined conjugates that are identical from batch to batch and simple to scale up and should allow for rapid and economic production of therapeutic antibodies for chronic disease therapy and Hesi et al teach Fab, Fab' and Fab-SH fragments for the treatment of inflammatory disorders wherein the antibody fragments may be conjugated to a polyethylene glycol (PEG) molecule via a cysteine residue in the light or heavy chain of the antibody fragment that would ordinarily form the disulfide bridge linking the light and heavy chains wherein the disulfide bridge is avoided by substituting one of the interchain cysteines for another amino acid, such as serine, wherein each PEG molecule may be 20,000 Da or 30,000 Da as well as pharmaceutical compositions comprising the antibody fragments and a pharmaceutically acceptable carrier, excipient or stabilizer and Humphreys teach known Fab' hinge region peptides (identical to instantly claimed SEQ ID Nos:1-3), which are well tolerated in *E.coli* and are non-immunogenic. Thus, it would have been *prima facie* obvious to one of

ordinary skill in the art at the time the claimed invention was made to have produced Fab or Fab' fragments comprising a hinge region having one or two cysteines (e.g., SEQ ID Nos:1-3) and wherein one or the interchain cysteines (CH1 or CL) is mutated to a serine and wherein the hinge cysteine(s) and the interchain cysteine (CH1 or CL) are PEGylated, as well as pharmaceutical compositions comprising the PEGylated Fab or Fab' fragments and a pharmaceutically acceptable carrier or excipient for therapeutic benefit of inflammatory disorders in view of claims 7 and 10 of U.S. Patent No. 6,642,356 B1 and Chapman et al and Hesi et al and Humphreys.

Claims 24-25, 27-29, 43, 45-46 and 48-56 are directed to an invention not patentably distinct from claims 7 and 10 of commonly assigned U.S. Patent No. 6,642,356 B1. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 6,642,356 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

20. Claims 5-7 are free of the prior art.

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643